**Hypothesis**

# EUKARYOTIC MESSENGER RNA AND INFORMOSOMES

*Omnia mea mecum porto*

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## 1. Introduction

Messenger RNA in eukaryotic cells is always complexed with protein, i.e., exists in the nucleoprotein form. The nucleoprotein form of eukaryotic mRNA was first discovered as the temporarily non-translatable (not bound with ribosomes) mRNA of the cytoplasm of early fish embryos [1] and that of sea urchins [2]. The ribonucleoprotein particles of a non-ribosomal nature were denoted as informosomes. Later, cytoplasmic informosomes were found in many other animal cells (reviewed [3,4]), as well as in higher plants [5]. Their characteristic features were always a high protein:RNA ratio (3:1) and a corresponding unique low buoyant density of CsCl (1.4 g/cm$^3$).

Shortly after, nuclear non-translatable mRNA precursors were also shown to exist in the form of nucleoproteins [6], with a number of properties in common with the cytoplasmic informosomes [7]. Further, translatable mRNA within polyribosomes also proved to be complexed with protein; dissociation of polyribosomes resulted in the release of messenger ribonucleoproteins resembling informosomes [8,9]. Finally, a special class of free proteins, capable of complexing with RNA and forming strictly stoichiometric informosome-like particles, were found in the cytoplasm of eukaryotic cells [3,10–12].

The biological meaning of the existence of eukaryotic mRNA or its nuclear precursors in the nucleoprotein form was not clear. A hypothesis was proposed that free cytoplasmic informosomes are a masked (stored, temporarily non-translatable) form of mRNA [1,3,13] and lately experimental support of this hypothesis was reported [14–18]. It was also suggested that the nucleoprotein form could be important for the transport of mRNA from the nucleus to the cytoplasm [1,3,7]. Further, bound protein could play a stabilizing and protective role for mRNA in the cell [3]. Finally, the presence of repressory and activatory RNA-binding proteins in the free state and in a complex with mRNA could ensure the effective and diversified regulation of protein synthesis at the translation level [3,4].

The observations described in the two following communications [19,20] have induced a new concept, which is expressed in the subtitle of this paper. It covers both the experimental facts described and all the above-mentioned hypothetical possibilities.

## 2. Formulation of the concept

In the two following papers it is shown that both in animal and plant cells at least some of the initiation and elongation factors of translation are RNA-binding proteins [19,20]. From this, I propose the hypothesis that:

1. RNA-binding activity is generally characteristic of many eukaryotic proteins having something to do with RNA and RNA-dependent processes.

2. Protein moiety of messenger ribonucleoproteins and informosomes consists of the RNA-binding proteins of this kind.

In connection with this, it can be thought that the protein moiety of free cytoplasmic informosomes and polyribosomal messenger ribonucleoproteins consists of proteins serving translation, including both the initiation, elongation and termination factors themselves and various regulators. Thus, in addition to the set of translation factors, free informosomes can contain special protein components which repress and mask mRNA. It is likely that some enzymes responsible for modifications of the translation factors, mRNA itself and bound regulatory proteins can also be included in the protein moiety of free informosomes or polyribosomal messenger ribonucleoproteins.

In the light of this concept, nuclear ribonucleoproteins of the informosome type must have another set of proteins. If the above-mentioned principle is obeyed, proteins of the nuclear particles must ensure modifications of the newly synthesized mRNA precursors, their processing and mRNA transport from the nucleus. Indeed, nuclear ribonucleoproteins were shown to contain specific RNAase-cleaving high molecular-weight RNA into large fragments [21], and poly(A)-polymerase responsible for the addition of poly(A)-sequences to the 3′-termini of RNA [22]. Data were reported suggesting the possible role of poly(A)-specific protein of the nuclear ribonucleoproteins in the transfer of mRNA from the nucleus into the cytoplasm [23]. It cannot be excluded that the existence of pre-mRNA in the nucleus and its transport is served also by the main protein component of nuclear ribonucleoproteins called 'informofer' [7], with polypeptide chains of approx. mol. wt 40 000 [24].

Thus, according to the concept proposed, the mRNA in eukaryotic cells carries on itself the proteins which are required for its own biogenesis, existence and functioning. These proteins are capable of binding with RNA and forming ribonucleoprotein particles of the informosome type.

## 3. Discussion

The binding with RNA of eukaryotic proteins which are involved in mRNA biogenesis and functions can hardly be interpreted as weak non-specific polyelectrolyte interactions or as mechanical occlusion. In the first place, RNA-binding proteins were found to bind RNA and polyribonucleotides very tightly (binding constants in the range $10^7$–$10^{13}$ $M^{-1}$) [25]. Secondly, the RNA–protein complexes formed are characterized by a unique and constant stoichiometry (protein:RNA = 3:1, by wt); their density distribution in CsCl is very narrow and specific, corresponding to the buoyant density of the particles of 1.4 g/cm$^3$ [10–12,26,27]. Exactly the same stoichiometry and buoyant density is characteristic for the cytoplasmic informosomes [3–5] and the nuclear ribonucleoprotein particles [7]. Thus, eukaryotic RNA-binding proteins seem to be specially fitted to function in the formation of special ribonucleoprotein particles of the informosome type.

The evolutionary acquisition of the RNA-binding function by proteins participating in mRNA biogenesis and translation can be directly connected with the necessity of concentrating these proteins near the sites of their functioning in the big eukaryotic cell. The volume of an eukaryotic cell is about three orders of magnitude greater than that of a prokaryotic cell. Therefore, while a prokaryotic cell can ensure the effective functioning of biological macromolecules by the processes of free diffusion and random collisions in the relatively small volume of its protoplasm, the big volumes of eukaryotic cells must inevitably require special systems of macromolecular transport, communications and compartmentation. The ability of functionally connected macromolecules to form specific physical complexes and aggregates can be considered as one of the simplest ways of compartmentation. In particular, to avoid high dilution and many unnecessary collisions in the big volume of eukaryotic protoplasm, the proteins functionally serving mRNA at the different stages of its life history must possess also the special capability to physically interact (bind) with RNA, thus forming ribonucleoproteins.

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